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# NONAQUEOUS TITRATIONS

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In recent years, an increasing number of papers have appeared on nonaqueous titrimetry. This aspect of analytical chemistry is still in its infancy and offers a tremendously helpful and handy tool to chemists. Short discussions of some of the various theories proposed for the behavior of acids and bases have been made by Fritz (1) and by Davis (2). Generally, the Brönsted theory is the one most applicable to nonaqueous titrimetry. The fact that the intrinsic strength of acids and bases is relative is probably the most important concept in this field. In the customary aqueous acid-base relationships, it is found that acids and bases of different inherent strengths act as though they were of the same strength. This phenomenon is called a "leveling effect." This leveling property is present in a system whenever: (a) a solvent is capable of an amphoteric nature towards a dissolved acid or base, or (b) the dissolved acid or base molecule contains two or more similar functional acidic or basic groups which are not widely different in strength.

In general, the basic or acidic properties of a molecule in a nonaqueous titration can be enhanced or suppressed in the direction desired by the proper choice of solvent, titrant, and indicator system. The influence of a solvent upon the acidity or basicity of various compounds can best be illustrated by the following observations: In glacial acetic acid, perchloric acid is completely dissociated into ions, whereas hydrogen chloride is not; in water, both perchloric acid and hydrogen chloride react as though they are completely ionized and acetic acid does not; and in a solvent, such as *n*-butylamine, all three acids appear to be completely dissociated.

The titration of a large number of different compounds as bases has been reported. Some of these are amino acids (3), amine hydrohalides (4), amine picrates (5), theobromine (6), various alkaloids (7), various aliphatic amines and nitrogen heterocycles (8), ethylenic compounds (9), tertiary amines (10), Schiff bases (11), aromatic amines (1, 12,13), and mixtures of various amines (14). Although these organic bases are primarily amines of one type or another, the diverse compounds titrated as acids are not limited to carboxylic acids. Some of the different organic substances which have been reported are: certain salts (15); enols and imides (16-18); carboxylic acids, acid chlorides, acid anhydrides, mercaptans, amine salts, and some nitro compounds (17); phenols (18-21); phenolic esters (22); nitroguanidine derivatives (23); "RDX" (hexahydro-1,3,5-trinitro-*s*-triazine) (24); and sulfa drugs and sulfonamides (25). A recent paper (26) gives a comprehensive bibliography and a review of nonaqueous titrimetry.

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## Nonaqueous Titration of Organic Bases

Conant and co-workers (27) carried out some of the early work on the titration of bases in acetic acid. Others (1,4, 6, 10,28,29) have used this same solvent. Fritz (1,12,13,29) has used various solvents, such as chlorobenzene, benzene, acetonitrile, chloroform, nitrobenzene, nitromethane, and ethyl acetate. Glycols (30), dioxane (8), and various alcohols (31) have also been used. The choice of a solvent for a given base is dependent upon (1) the solubility of the base, (2) the inherent strength of the base relative to the titrant acid, (3) the sharpness of the end-point obtainable, (4) the coincidence of a visual indicator end-point with the potentiometric end-point, (5) the nonreactivity of the base with the solvent, and (6) the cost and ready availability of the solvent in a usable form. The general order of basicity for amines is primary > secondary > tertiary, and aliphatic > heterocyclic > aromatic. There are numerous exceptions to these orders of strength which can only be determined through experience. Usually, the sharpness of an end-point for similar amines in a given solvent and titrant system increases as the basic strength increases. The sharpness of an end-point can often be increased by decreasing the polarity of the solvent (32) by the addition of small amounts of solvents, such as cyclohexane or ligroine.

The most commonly used titrant for bases is 0.01 to 0.1 *N* perchloric acid in glacial acetic acid or in *p*-dioxane. Perchloric acid is the strongest common acid known and will give a neutralization with practically all bases. Phthalic acid monopotassium salt is an excellent primary standard for this acid. Davis and Hetzer (33) have reported the use of diphenyl phosphate, which is a solid and can be weighed directly without the need of a primary standard, but this acid is much weaker than perchloric and is thus more limited.

Numerous methods are available for detecting the end-point in a nonaqueous titration of a base. Photometric methods (10) have been used, but in the majority of the work reported to date visual indicators and potentiometric determinations of end-point have been employed. The most widely used electrode systems for the titration of bases are the glass *versus* calomel and glass *versus* silver-silver chloride combinations. This latter pair is useful in practically all of the solvents used in this work. It is not possible to duplicate exactly the end-point voltage of a titration with either electrode combination, but this failure does not lessen the value of potentiometric titrations and is probably due to the nature of the glass electrode. The use of visual indicators is the most convenient means of detecting an end-point in solutions which are not colored, but the coincidence of an indicator color change with the potentiometric end-point must always be checked before an indicator is used. Methyl violet and crystal violet have been used extensively in the titration of bases (1,12,28). Both of these indicators exhibit the following color changes as one proceeds from the basic to the acidic forms of the indicators: purple to blue to blue-green to green to green-yellow to yellow. Any one of these color changes may be the change which corresponds to the equivalence point in a titration (28). The agreement of any particular color change with the equivalence point is controlled by the nature of the solvent system and the base being titrated. Other indicators which have been reported are 1-naphtholbenzein, neutral red, dibenzalacetone, triphenylmethanol, methyl red, modified methyl orange, and tetrabromophenolphthalein ethyl ester (2,8,29).

## Nonaqueous Titration of Organic Acids

Generally, the same rules apply for the selection of a solvent for the titration of an organic compound as an acid as are given in the preceding section for

the selection of a solvent for a base. Ethylenediamine and *n*-butylamine (16-21) are used as solvents for the very weakly acidic compounds, such as phenols and enols. Since these two solvents are strong bases, they enhance the acidic properties of a weakly acid material. Dimethylformamide and pyridine are somewhat weaker bases than ethylenediamine and *n*-butylamine, and are used as solvents for the acidic compounds of intermediate strength. Strongly acidic materials, such as carboxylic acids, acid chlorides, and acid anhydrides, can be titrated in any of these four solvents if there is no reaction between the solvent and the solute, but essentially inert solvents, such as methanol, benzene-methanol mixtures, ether, acetonitrile, and acetone, can also be used, because of the greater relative acid strength of these acids. Often both a weak acid and a strong acid in a mixture can be determined by two titrations. In one titration, a nonbasic solvent is used and only the strong acid is titrated. In a second titration, a basic solvent is used and both acids are determined (16,19); the amount of the weaker acid is then obtained by taking the difference between the two results.

The use of 0.1 to 0.2 *N* solutions of sodium methoxide or potassium methoxide in methanol and benzene has been applied most frequently in the titration of acidic materials (16-19). The use of the potassium reagent offers definite advantages over sodium methoxide. First of all, a solution of potassium methoxide can be prepared by using almost twice as much benzene in relation to the methanol as can be used in preparing the sodium reagent. The presence of methanol (an extremely weak acid) levels or decreases the apparent acid strength of a weak acid towards a methoxide base; thus, the lesser amount of methanol required to keep potassium methoxide in solution makes this reagent react as a much stronger base than the sodium methoxide. In addition, potassium methoxide can be used with an electrode system containing the glass electrode. Sodium ions, when present in high concentration, accumulate in the glass electrode and cause it to act erratically, thus preventing the use of this electrode with sodium methoxide in nonaqueous titrations. A recent paper (20) has reported the use of alcoholic potassium hydroxide and of tetrabutylammonium hydroxide as titrants in this work. Benzoic acid is a commonly used primary standard for these basic titrants.

The detection of end-points in the nonaqueous titration of acidic compounds can be carried out potentiometrically (17,20) with the aid of a visual indicator (15-17) or by high-frequency methods (18,21). Electrode combinations of glass *versus* calomel, calomel *versus* antimony, and antimony *versus* antimony have been used predominantly. The number of visual indicators which have been applied to this method are rather limited in number. *o*-Nitroaniline (16) has been about the only successful indicator found for the titration of very weak acids, such as phenols. Its use is limited to work in ethylenediamine. *p*-Nitrobenzeneazo-resorcinol (azo violet) and thymolsulfonephthalein (thymol blue) are the two most popular indicators. Azo violet is normally used for acids of intermediate strengths in dimethylformamide or ethylenediamine. Thymol blue has a color change which occurs more on the acid side than that of azo violet, and is thus used for intermediate and strong acids. Most of the literature records a clear blue color as the end-point color for both azo violet and thymol blue with various compounds. Kaye (24) has reported a green end-point for the titration of RDX with sodium methoxide in dimethylformamide using azo violet. It has been the experience of this author that both azo violet and thymol blue may give blue, green, yellow-green, brownish-green, or brown end-point colors. The color ob-

tained with a particular indicator seems to be dependent upon the compound being titrated and, to a lesser degree, upon the solvent system used.

The accuracy and precision obtainable in the nonaqueous titration of either acids or bases are excellent. The accuracy approaches 100% and the precision is generally of the order of ±0.3%, depending upon the various factors which are encountered for each compound. This method of analysis provides a rapid means of assaying a very large number of organic compounds, it provides a method for determining accurate equivalent weights, and is helpful in following the rate of a reaction carried out in a nonaqueous medium.

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